REMARKS

The Office Action mailed March 6, 2001 presents the examination of claims 1-40. These claims are deemed free of the prior art. Claims 1-31, and 34-41 are pending. Claims 32 and 33 have been cancelled. Claims 1, 4, 7, 10, 15, 22, 23, 24, 27, 28, 29, 30, 31, 34, 35, 37, 38, 39 and 40 have been amended. New claim 41 has been added.

The specification has been amended in view of the Sequence Listing attached hereto to incorporate Sequence Listing identifiers as required under 37 C.F.R. § 1.821(d). Also accompanying the present Amendment is a Substitute Specification in both clean and mark-up versions incorporating those amendments for the convenience of the Examiner.

The above amendments to the specification and claims do not introduce new matter to the application as filed.

This Amendment is also accompanied by a computer readable form of the Sequence Listing (CRF). The Sequence Listing on the CRF is identical to the printed copy of the Sequence Listing attached hereto.

Support for New Claim

New claim 41 describes cloning using the method of the present invention together with a nucleic hybridization approach. Claim 41

finds support in the specification at, for example, page 11, lines 19-27.

Rejections Under 35 U.S.C. § 112, Second Paragraph

Claims 1-40 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for reasons set forth on pp. 3-9 of the Office Action. Applicants submit that the amendments to the claims made herein address all of the bases put forward for this rejection except:

1. The use of the term "identifying" in claims 1-28, 37-40;

2. The use of the terms "selecting" and "substituting" in claims 29-36;

3. The use of the term "desired amino acid sequence" in claims 29-36;

4. The use of the term "corresponding" or "correspondence" in claims 1-28 and 37-40;

5. The use of the term "the preferred codon" in claims 29-36; and

6. The lack of relation back to the preamble in claims 30 and 36.

With regard to "identifying", Applicants understand that the Examiner is suggesting that the act of identifying something is somehow not an active step. Applicants submit to the contrary that

"identifying" an amino acid sequence as being one that is a conserved portion of a polypeptide is in fact an active step.

Consideration of concrete examples may clarify this. It makes no difference to the present invention whether one makes this identification by inspecting sequences visually and making a conscious decision (a process perhaps considered "mental" in character) or makes this identification by manipulating data with a computer program and utilizing the output of the program (a process clearly "active"). Thus, it is seen that activity on the part of the practitioner, whether "mental" or otherwise, is part of "identifying" and thus a step of "identifying" is an "active" step.

Similarly, Applicants submit that the terms "selecting" and "substituting" are also active steps. Applicants acknowledge that these terms have more of a "mental" character, than a term such as "heating" or the like. However, this does not establish that these terms are not active steps. The terms "selecting" and "substituting" clearly state what the practitioner is doing at each of these steps of the process. Applicants submit that the present terms should be held up in contrast to the more generic term "using x to accomplish y" or the like, or a term such as "selection", which terms are indeed typically deemed indefinite for not reciting an active step.

The Examiner also objects to use of the term "corresponding" or "correspondence". Applicants submit that one of ordinary skill in the art would understand what is meant by these terms and they are in

no way indefinite. "Corresponding" residues are generally known in the art of molecular biology as being residues in the same position in an alignment of two sequences. An example of "correspondence" among residues is provided at page 9, lines 1-22 of the specification.

The Examiner objects to the term "desired amino acid sequence", indicating that it is not clear what distinguishes a desired sequence from any other. Applicants submit that the term "desired" is a label of convenience to point out that amino acid sequence as an object of attention. Thus, a "desired amino acid sequence" is distinct from all others in that it is the one the practitioner wishes to manipulate or isolate or the like. Applicants submit that this is not indefinite claim language.

The term "the preferred codon" is actually "the most preferred codon" in claims 26-30. Applicants submit that the construction "a most preferred codon" would be incorrect, as there can be only one "most preferred codon". Thus, use of the definite article is proper in this case.

Finally, the Examiner alleges a lack of correlation between the preamble of claims 30 and 36 and the final steps of these claims. Claim 36 in its original form inadvertantly included claim 30 in its dependency. The present amendment addresses this issue as to claim 36. In claim 30 the preamble recites a method of "preparing" an oligonucleotide, while the final step recites "synthesizing" an

oligonucleotide. Applicants submit that the claimed method is not directed to an actual synthetic method, in the sense that a particular method for polymerizing monomers or the like is not the object of the invention. Rather, the claim is directed to an overall method for preparing an oligonucleotide having desirable characteristics as recited in the claim. The method of preparation includes two basic steps, a design step and a synthesis step. The end result of the synthesis is in fact an oligonucleotide. Applicants submit that the lack of exact correspondence of language of the preamble and last step does not render claim 30 indefinite.

For all of the above reasons, Applicants submit that the instant rejection of claims 1-40 under 35 U.S.C. § 112, second paragraph, should be withdrawn.

If there are any minor matters precluding allowance of the application which may be resolved by a telephone discussion, the Examiner is respectfully requested to contact Mark J. Nuell, Ph.D. (Reg. No. 36,623) at (703) 205-8000.

Pursuant to 37 C.F.R. § 1.17 and 1.136(a), Applicants respectfully petition a three (3) month extension of time for filing a response in connection with the present application. Please charge the required fee of $445.00 to Deposit Account No. 50-1055.

If the Primary Deposit Account No. 50-1055 is deficient and non-payment will result in a loss of rights, the Commissioner is hereby authorized in this, concurrent and future replies, to charge payment

to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17; particularly, extension of time fees.

Respectfully submitted,

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By _____
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Attachments:
Version Showing Marked-up Copy of Amendments
Sequence Listing (Printed Copy and CRF)
Copy of Notice to Comply
Marked-up Copy of Substitute Specification Showing Changes Made
Clean Copy of Substitute Specification

VERSION SHOWING MARKED-UP COPY OF AMENDMENTS

In the Specification:

The Specification has been amended at pages 20-25. Please refer to the attached marked-up Substitute Specification.

In the Claims:

Claims 32 and 33 have been cancelled.

Claims 1, 4, 7, 10, 15, 22, 23, 24, 27, 28, 29, 30, 31, 34, 35, 37, 38, 39 and 40 have been amended, as shown on the attached pages.

New claim 41 has been added.

1. (Amended) A method for isolating from a target plant species a target polynucleotide encoding a target polypeptide comprising a conserved region exhibiting at least 70% sequence identity to a conserved region of template polypeptide that is encoded by a template polynucleotide from a template plant species, comprising:

(a) identifying an amino acid sequence of a conserved region in the template polypeptide;

(b) generating an oligonucleotide comprising a sequence wherein the sequence or its reverse complement comprises at least four codons that encode a portion of the amino acid sequence of (a), wherein

(i) the sequence of the first and second positions of at least three of the codons is the same as ~~the~~ corresponding nucleotides in nucleotides in the template polynucleotide;

(ii) the nucleotide at the third position of the codons of (i) is the nucleotide of the third position of ~~the~~a most preferred codon of the target plant class for ~~the~~a desired amino acid;

(c) contacting the oligonucleotide with a composition comprising the target polynucleotide under conditions that permit hybridization of the oligonucleotide to the target polynucleotide to form a duplex; and

(d) isolating the ~~duplex.~~ duplex comprising the target polynucleotide.

2. The method of claim 1, wherein the oligonucleotide does not contain a homopolymer of more than four guanine or cytosine residues.

3. The method of claim 1, wherein the oligonucleotide does not contain a homopolymer of more than four residues.

4. (Amended) The method of claim 1, wherein ~~wherein the sequence or~~ wherein the sequence or the oligonucleotide of step (b) or its reverse complement further comprises at least one codon wherein

(i) the sequence of the first and second position of the codon is the same as~~the~~ corresponding nucleotides in the template polynucleotide;

(ii) the sequence of the third position of the codon of step (I) is the same as the nucleotide of the third position of ~~the~~a second most preferred codon of the target plant species for ~~the~~a desired amino acid; and

(iii) the oligonucleotide is not degenerate.

5. The method of claim 1, wherein the target polynucleotide is from a monocot plant and the template polynucleotide is from a dicot plant.

6. The method of claim 4, wherein the template polynucleotide is from Arabidopsis.

7. (Amended) The method of claim 5, wherein the third position of each codon of the oligonucleotide is either a guanosine or cytosine.

8. The method of claim 2, wherein both the template and target polynucleotides are from dicot plants.

9. The method of claim 8, wherein the template polynucleotide is from Arabidopsis.

10. (Amended) The method of claim 9, wherein the third position of each codon of the oligonucleotide is either an adenosine or thymidine.

11. The method of claim 1, wherein the template polynucleotide is from a monocot plant and the target polynucleotide is from a dicot plant.

12. The method of claim 1, wherein both the template and target polynucleotides are from monocot plants.

13. The method of claim 11 or 12, wherein the template polynucleotide is from corn.

14. The method of claim 12, wherein the target polynucleotide is from corn.

15. (Amended) The method of claim 1, wherein step (a) comprises aligning the sequences of polynucleotides of plants within a family and identifying a portion of the template polynucleotide that exhibits at least 70% sequence identity to a portion of a polynucleotide from a plant of a genus closely related to the plant from which the template polynucleotide originates.

16. The method of claim 1, wherein step (a) comprises identifying the primary sequence in a region of the template polypeptide sequence that forms a secondary structure.

17. The method of claim 16, wherein the secondary structure is a helix or a beta sheet.

18. The method of claim 1, wherein the conserved region is a motif or functional domain.

19. The method of claim 1, wherein step (a) comprises identifying the primary sequence in a region of the template polypeptide that is repeated.

20. The method of claim 1, wherein the oligonucleotide comprises from 6 to 11 codons.

21. The method of claim 1, wherein step (c) further includes contacting the composition comprising the target polynucleotide with a second oligonucleotide, wherein the second oligonucleotide is a degenerate oligonucleotide encoding a second portion of the conserved region.

22. (Amended) A method of isolating from a target organism a target polynucleotide encoding a conserved region in a template polypeptide encoded by a template polynucleotide comprising:

(a) identifying the amino acid sequence of the conserved region in the template polypeptide;

(b) generating an oligonucleotide comprising a sequence wherein the sequence or its reverse complement comprises at least four codons that encode a portion of the conserved region of step (a), wherein

(i) the sequence of the first and second positions of at least three codons is the same as ~~the~~ corresponding nucleotides in the template polynucleotide;

(ii) the nucleotide of the third position of ~~those six~~the at least three codons of the oligonucleotide is the same nucleotide in the third position of the most preferred codon of the target ~~plant species~~organism for the desired amino acid;

(iii) the oligonucleotide does not comprise homopolymers of more than four nucleotides; and

(iv) the oligonucleotide is not degenerate;

(c) contacting the oligonucleotide with a composition comprising the target polynucleotide under conditions that permit hybridization of the oligonucleotide to the target polynucleotide to form a duplex;

(d) contacting the duplex of step (c) with a thermostable polymerase under conditions to elongate the oligonucleotide of step (b); and

(e) isolating the elongation product of step ~~(d).~~ (d) as the target polynucleotide.

23. (Amended) A method for identifying in a target organism a target polynucleotide encoding a conserved region in a template polypeptide encoded by a template polynucleotide comprising:

(a) identifying the amino acid sequence of the conserved region in the template polypeptide;

(b) generating an oligonucleotide comprising a sequence wherein the sequence or its reverse complement comprises four codons that encode a portion of the conserved region of step (a), wherein

(i) the sequence of the first and second positions of at least three codons is the same as~~the~~ corresponding nucleotides in the template polynucleotide;

(ii) the nucleotide of the third position of ~~those six~~the at least three codons of the oligonucleotide is the same nucleotide in the third position of the most preferred codon of the target plant species for the desired amino acid;

(iii) the oligonucleotide does not comprise homopolymers of more than four nucleotides; and

(iv) the oligonucleotide is not degenerate;

(c) contacting the oligonucleotide with a composition comprising the target polynucleotide under conditions that permit hybridization of the oligonucleotide to the target polynucleotide to form a duplex;

(d) contacting the duplex of step (c) with a thermostable polymerase under conditions to elongate the oligonucleotide of step (b); and

(e) determining the nucleotide sequence of the elongation product of step ~~(d).~~

(d), thereby identifying the target polynucleotide.

24. (Amended) A method of isolating from a target plant species a target polynucleotide encoding a polypeptide of a conserved region in a template polypeptide encoded by a template polynucleotide, comprising:

(a) identifying the amino acid sequence of the conserved region in the template polypeptide;

(b) generating a first oligonucleotide comprising a sequence wherein the sequence or its reverse complement comprises four codons that encode a first portion of the conserved region of step (a), wherein

(i) the sequence of the first and second position of at least three codons is the same as~~the~~

corresponding nucleotides in the template polynucleotide;

(ii) the nucleotide of the third position of the codons of step (i) is the same as the nucleotide in the third position of the most preferred codon of the target plant species for the desired amino acid;

(iii) the oligonucleotide does not comprise homopolymers of more than four nucleotides; and

(iv) the oligonucleotide is not degenerate;

(c) generating a second oligonucleotide wherein its sequence or its reverse complement comprises four codons that encode a second portion of the conserved region of step (a), wherein

(i) the sequence of the first and second position of at least three codons is the same as ~~the~~ corresponding position in the template polynucleotide;

(ii) the nucleotide of the third position of those codons is the same as the nucleotide of the third position of the most preferred codon of the target plant species for the desired amino acid;

(iii) the oligonucleotide does not comprise homopolymers of more than four nucleotides; and

(iv) the oligonucleotide is not degenerate;

(d) contacting the first and second oligonucleotides with a composition comprising the target polynucleotide under conditions that permit hybridization of at least one of the oligonucleotides and the target polynucleotide to form a duplex;

(e) contacting the duplex of step (d) with a thermostable polymerase under conditions to elongate the at least one hybridized oligonucleotide;

(f) generating a strand complementary to the elongation product of step (e); and

(g) isolating the product of step ~~(d).~~

(f) as the target polynucleotide.

25. The method of claim 24, wherein the two oligonucleotide sequences or their reverse complements encode portions of the conserved region of step (a) that are separated by at least 30 amino acids.

26. The method of claim 24, wherein the two oligonucleotide sequences or their reverse complement encode between 6 to 11 amino acids of the conserved region of step (a).

27. (Amended) The method of claim 24, wherein the product of step ~~(f)~~ (g) is inserted into a vector.

28. (Amended) A method for identifying in a target plant species a target polynucleotide encoding a polypeptide of a conserved region in a template polypeptide encoded by a template polynucleotide, comprising:

(a) identifying the amino acid sequence of the conserved region in the template polypeptide;

(b) generating a first oligonucleotide comprising a sequence wherein the sequence or its reverse complement comprises four codons that encode a first portion of the conserved region of step (a), wherein

(i) the sequence of the first and second position of at least three codons is the same as ~~the~~ corresponding nucleotides in the template polynucleotide;

(ii) the nucleotide of the third position of the codons of step (i) is the same as the nucleotide in the third position of the most preferred codon of the target plant species for the desired amino acid;

(iii) the oligonucleotide does not comprise homopolymers of more than four nucleotides; and

(iv) the oligonucleotide is not degenerate;

(c) generating a second oligonucleotide wherein its sequence or its reverse complement comprises four codons that encode a second portion of the conserved region of step (a), wherein

(i) the sequence of the first and second position of at least three codons is the same as ~~the~~ corresponding position in the template polynucleotide;

(ii) the nucleotide of the third position of those codons is the same as the nucleotide of the third position of the most preferred codon of the target plant species for the desired amino acid;

(iii) the oligonucleotide does not comprise homopolymers of more than four nucleotides; and

(iv) the oligonucleotide is not degenerate;

(d) contacting the first and second oligonucleotides with a composition comprising the target polynucleotide under conditions that permit hybridization of at least one of the oligonucleotides and the target polynucleotide to form a duplex;

(e) contacting the duplex of step (d) with a thermostable polymerase under conditions to elongate the at least one hybridized oligonucleotide;

(f) generating a strand complementary to the elongation product of step (e); and

(g) determining the nucleotide sequence of the product of step ~~(f).~~

(f), thereby identifying the target polynucleotide.

~~29. A~~29. (Amended) A method for ~~selecting~~designing a nucleotide sequence ~~of~~for an oligonucleotide primer for a polymerase chain reaction comprising:

(a) selecting a nucleotide sequence encoding a desired amino acid sequence from a template organism, or the complement thereof;

(b) selecting for the nucleotide of the third position of each codon the preferred codon for a target organism, provided said nucleotide is guanine or cytosine;

~~(c) if~~(c) if the nucleotide of the third position of the preferred codon is adenine or thymine, then substituting either a guanine or cytosine, selecting guanine or cytosine to avoid introducing a poly-guanylate or polycytidylate sequence of more than four residues;

(d) thereby obtaining a nucleotide sequence for an oligonucleotide primer;

wherein said desired amino acid sequence is encoded by one reading frame, or a portion thereof, of the nucleotide sequence of said primer or the complement thereof.

30. (Amended) A method for preparing an oligonucleotide primer for a polymerase chain reaction comprising:

i) designing a nucleotide sequence by;

(a) selecting a nucleotide sequence encoding a desired amino acid sequence from a template organism, or the complement thereof;

(b) selecting for the nucleotide of the third position of each codon the preferred codon for a target organism, provided said nucleotide is guanine or cytosine;

(c) if the nucleotide of the third position of the preferred codon is adenine or thymine, then substituting either a guanine or cytosine, selecting guanine or cytosine to avoid introducing a poly-guanylate or polycytidylate sequence of more than four residues; and

~~(d) synthesizing said~~ii) synthesizing an oligonucleotide primer comprising the designed sequence, wherein said desired amino acid sequence is encoded by one reading frame, or a portion thereof, of the nucleotide sequence of said primer or the complement thereof.

31. (Amended) A method for cloning a nucleic acid comprising:

i) designing a pair of oligonucleotide primers by;

(a) selecting an upstream nucleotide sequence encoding a first desired amino acid sequence from a template organism and a downstream nucleotide sequence encoding a second desired amino acid sequence;

(b) for each of said upstream and downstream nucleotide sequences, selecting for the nucleotide of the third position of each codon the preferred codon for a target organism, provided said nucleotide is guanine or cytosine;

(c) if the nucleotide of the third position of the preferred codon is adenine or thymine, then substituting either a guanine or cytosine, selecting guanine or cytosine to avoid introducing a poly-guanylate or polycytidylate sequence of more than four residues.

ii) synthesizing an upstream oligonucleotide primer and a downstream oligonucleotide primer comprising the nucleotide sequences designed according to steps (b) and (c); and

iii) performing a polymerase chain reaction using said upstream and downstream primers and a template comprising a nucleic acid sample obtained from said target organism, thereby obtaining a cloned nucleic acid.

32. (**Cancel**) The method of claim 31, further comprising:

(d) synthesizing an upstream oligonucleotide primer, or a portion thereof according to steps (b) and (c).

33. (**Cancel**) The method of claim 32, further comprising:

(e) performing a polymerase chain reaction using said upstream and downstream primers and a template comprising a nucleic acid sample obtained from said target organism.

34. (Amended) The method of claim ~~33,~~ 31, further comprising:

~~(f) using the product of said polymerase chain reaction of step (c) as a probe to screen~~ (f) screening a library prepared from nucleic acids obtained from said target~~organism.~~

organism using the product of said polymerase chain reaction of step (e) as a probe .

35. (Amended) The method of claim ~~33,~~31, further comprising:

(f') inserting the product of the polymerase chain reaction of step (e) into a vector.

36. (Amended) The method of any one of claims ~~30-35,~~[30-35] 31, 34 or 35, wherein said template organism is a dicot and said target organism is a monocot or wherein said template organism is a monocot and said target organism is a dicot.

37. (Amended) A method for isolating a target polynucleotide encoding a target polypeptide comprising a conserved region of a template polypeptide that is encoded by a template polynucleotide, comprising:

(a) identifying an amino acid sequence of a conserved region in the template polypeptide;

(b) generating an oligonucleotide comprising a sequence wherein the sequence or its reverse complement comprises at least four codons that encode a portion of the amino acid sequence of (a), wherein

(i) the sequence of the first and second positions of at least three of the codons is the same as~~the~~ corresponding nucleotides in nucleotides in the template polynucleotide;

(ii) the nucleotide at the third position of the codons of (i) is the nucleotide of the third position of the most preferred codon of the target plant species for the desired amino acid;

(c) contacting the oligonucleotide with a composition comprising the target polynucleotide under conditions that permit hybridization of the oligonucleotide to the target polynucleotide to form a duplex; and

~~(d) generating~~elongating said oligonucleotide to form a single strand ~~polynucleotide.~~

(d) polynucleotide and isolating the elongation product as the target polynucleotide.

38. ~~A~~(Amended)A method for isolating ~~a~~ from a target plant species a target polynucleotide encoding a target polypeptide comprising a conserved region exhibiting at least 70% sequence identity to a conserved region of template polypeptide that is encoded by a template polynucleotide from a template plant species, comprising:

(a) identifying an amino acid sequence of a conserved region in the template polypeptide;

(b) generating an oligonucleotide comprising a sequence wherein the sequence or its reverse complement comprises at least four codons that encode a portion of the amino acid sequence of (a), wherein

(i) the sequence of the first and second positions of at least three of the codons is the same as~~the~~ corresponding nucleotides in nucleotides in the template polynucleotide;

(ii) the nucleotide at the third position of the codons of (i) is the nucleotide of the third position of the most preferred codon of ~~the~~a plant family of target plant species for the desired amino acid;

(c) contacting the oligonucleotide with a composition comprising the target polynucleotide under conditions that permit hybridization of the oligonucleotide to the target polynucleotide to form a duplex; and

(d) isolating the ~~duplex.~~ duplex, thereby isolating the target polynucleotide.

39. (Amended) A method for isolating~~a~~ from a target plant species a target polynucleotide encoding a target polypeptide comprising a conserved region exhibiting at least 70% sequence identity to a conserved region of template polypeptide that is encoded by a template polynucleotide from a template plant species, comprising:

(a) identifying an amino acid sequence of a conserved region in the template polypeptide;

(b) generating an oligonucleotide comprising a sequence wherein the sequence or its reverse complement comprises at least four codons that encode a portion of the amino acid sequence of (a), wherein

(i) the sequence of the first and second positions of at least three of the codons is the same as~~the~~ corresponding nucleotides in nucleotides in the template polynucleotide;

(ii) the nucleotide at the third position of the codons of (i) is the nucleotide of the third position of the most preferred codon of ~~the plant genera for~~a genus of the target plant species for the desired amino acid;

(c) contacting the oligonucleotide with a composition comprising the target polynucleotide under conditions that

isolating the

(d) duplex, thereby isolating the target polynucleotide.

40. (Amended) A method for isolating~~a~~ from a target plant species a target polynucleotide encoding a target polypeptide comprising a conserved region exhibiting at least 70% sequence identity to a conserved region of template polypeptide that is encoded by a template polynucleotide from a template plant species, comprising:

(a) identifying an amino acid sequence of a conserved region in the template polypeptide;

(b) generating an oligonucleotide comprising a sequence wherein the sequence or its reverse complement comprises at least four codons that encode a portion of the amino acid sequence of (a), wherein

(i) the sequence of the first and second positions of at least three of the codons is the same as ~~the~~ corresponding nucleotides in nucleotides in the template polynucleotide;

(ii) the nucleotide at the third position of the codons of (i) is the nucleotide of the third position of the most preferred codon~~of the plant species~~ of the target plant species for the desired amino acid;

(c) contacting the oligonucleotide with a composition comprising the target polynucleotide under conditions that permit hybridization of the oligonucleotide to the target polynucleotide to form a duplex; and

(c) ~~(d) isolating the duplex.~~isolating the duplex, thereby isolating the target polynucleotide.